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2 CLAIMS
3

4 1. A method of treating rhinosinusitis or alleviating the symptoms of rhinosinusitis,
5 comprising
6 administering an agent that permits the release of proteins from the endoplasmic
7 reticulum.
8

9 2. The method of claim 1, wherein the agent is delivered intranasally.
10

11 3. The method of claim 1, further comprising the step of:
12 providing an individual suffering from rhinosinusitis.
13

14 4. The method of claim 3, wherein the providing step comprises providing an individual
15 suffering from chronic rhinosinusitis.
16

17 5. The method of claim 3, wherein the individual carries a mutation in at least one copy
18 of a gene encoding a cystic fibrosis transmembrane conductance regulator.
19

20 6. The method of claim 3, wherein the gene is the *CFTR* gene.
21

22 7. The method of claim 3, wherein the individual carries a mutation in one copy of the
23 gene.
24

25 8. The method of claim 3, wherein the individual carries a mutation in both copies of
26 the gene.
27

28 9. The method of claim 7 or claim 8, wherein the mutation is a $\Delta F508$ mutation.
29

30 10. The method of claim 9, wherein the individual carries an M470V variant of the
31 *CFTR* gene.
32

33 11. A method of treating hemochromatosis or alleviating the symptoms of
34 hemochromatosis, comprising

1 administering an agent that permits the release of proteins from the endoplasmic
2 reticulum.
3
4 12. The method of claim 11, further comprising the step of:
5 providing an individual suffering from hemochromatosis.
6
7 13. The method of claim 11, wherein the providing step comprises providing an
8 individual having a mutation in at least one copy of a gene encoding an HFE protein.
9
10 14. The method of claim 12, wherein the individual carries a mutation in one copy of
11 the gene.
12
13 15. The method of claim 12, wherein the individual carries a mutation in both copies of
14 the gene.
15
16 16. A method of treating Gitelman's syndrome or alleviating the symptoms of
17 Gitelman's syndrome, comprising
18 administering an agent that permits the release of proteins from the endoplasmic
19 reticulum.
20
21 17. The method of claim 16, further comprising the step of:
22 providing an individual suffering from Gitelman's syndrome.
23
24 18. The method of claim 17, wherein the individual carries a mutation in at least one
25 copy of a gene encoding a thiazide sensitive Na-Cl cotransporter.
26
27 19. The method of claim 18, wherein the gene is the *NCC* gene.
28
29 20. The method of claim 19, wherein the mutation is a G738R mutation.
30
31 21. The method of claim 18, wherein the individual carries a mutation in one copy of
32 the gene.
33

- 1 22. The method of claim 18, wherein the individual carries a mutation in both copies of
2 the gene.
3
- 4 23. A method of treating cystinuria or alleviating the symptoms of cystinuria,
5 comprising administering an agent that permits the release of proteins from the
6 endoplasmic reticulum.
7
- 8 24. The method of claim 23, further comprising the step of:
9 providing an individual suffering from cystinuria.
10
- 11 25. The method of claim 24, wherein the providing step comprises providing an
12 individual suffering from type I cystinuria.
13
- 14 26. The method of claim 24, wherein the individual carries a mutation in at least one
15 copy of a gene encoding a subunit of an rBAT protein.
16
- 17 27. The method of claim 26, wherein the individual carries a mutation in one copy of
18 the gene.
19
- 20 28. The method of claim 26, wherein the individual carries a mutation in both copies of
21 the gene.
22
- 23 29. The method of any of claims 3, 12, 17, or 24, wherein the agent is a calcium pump
24 inhibitor.
25
- 26 30. The method of any of claims 3, 12, 17, or 24, wherein the agent decreases or
27 inhibits the activity of UDP glucose:glycoprotein glycosyl transferase.
28
- 29 31. The method of any of claims 3, 12, 17, or 24, wherein the agent decreases or
30 inhibits activity of the endoplasmic reticulum Ca^{++} ATPase.
31
- 32 32. The method of any of claims 3, 12, 17, or 24, wherein the agent lowers the
33 concentration of Ca^{++} in the endoplasmic reticulum.
34

- 1 33. The method of any of claims 3, 12, 17, or 24, wherein the agent causes release of
2 Ca^{++} from the endoplasmic reticulum.
3
- 4 34. The method of any of claims 3, 12, 17, or 24, wherein the agent stimulates or
5 increases IP_3 receptor activity.
6
- 7 35. The method of any of claims 3, 12, 17, or 24, wherein the agent decreases or
8 inhibits calnexin functional activity
9
- 10 36. The method of any of claims 3, 12, 17, or 24, wherein the agent increases or
11 activates ryanodine receptor activity
12
- 13 37. The method of any of claims 3, 12, 17, or 24, wherein the agent comprises
14 thapsigargin or a derivative thereof.
15
- 16 38. The method of any of claims 3, 12, 17, or 24, wherein the agent comprises DBHQ
17 or a derivative thereof.
18
- 19 39. The method of any of claims 3, 12, 17, or 24, wherein the agent comprises
20 cyclopiazonic acid or a derivative thereof or wherein the agent comprises halothane or a
21 derivative thereof.
22
- 23 40. The method of any of claims 3, 12, 17, or 24, wherein the agent permits release
24 of mis-assembled or mis-folded proteins from the endoplasmic reticulum.
25
- 26 41. The method of any of claims 3, 12, 17, or 24, wherein the agent is an
27 oligonucleotide which is antisense to a protein selected from the group consisting of
28 UDP glucose:glycoprotein glycosyl transferase, calnexin and Ca^{++} ATPase.
29
- 30 42. A method of treating any disease or clinical condition, comprising
31 administering an agent that permits the release of proteins from the endoplasmic
32 reticulum, wherein the agent increases or activates ryanodine receptor activity.
33
- 34 43. The method of claim 42, wherein the disease is selected from the list consisting of:

- 1 Cystic Fibrosis, Chronic Obstructive Pulmonary Disease, Paroxysmal Nocturnal
- 2 Hemoglobinuria, Familial Hypercholesterolemia, Tay-Sachs Disease, viral diseases,
- 3 neoplastic diseases, Hereditary Myeloperoxidase Deficiency, Congenital Insulin
- 4 Resistance, Rhinosinusitis, Nephrogenic Diabetes Insipidus, Hemochromatosis,
- 5 Gitelman's Syndrome, and Cystinuria.
- 6
- 7 44. A method of releasing a mis-assembled or mis-folded glycoprotein from the
- 8 endoplasmic reticulum of a cell comprising the step of administering an agent that
- 9 decreases or inhibits the functional activity of UDP glucose:glycoprotein glycosyl
- 10 transferase.
- 11
- 12 45. A method of releasing a mis-assembled or mis-folded glycoprotein from the
- 13 endoplasmic reticulum of a cell comprising the step of administering an agent that
- 14 decreases or inhibits activity of the endoplasmic reticulum Ca^{++} ATPase.
- 15
- 16 46. A method of releasing a mis-assembled or mis-folded glycoprotein from the
- 17 endoplasmic reticulum of a cell comprising the step of administering an agent that
- 18 lowers the concentration of Ca^{++} in the endoplasmic reticulum.
- 19
- 20 47. A method of releasing a mis-assembled or mis-folded glycoprotein from the
- 21 endoplasmic reticulum of a cell comprising the step of administering an agent that
- 22 decreases or inhibits calnexin functional activity.
- 23
- 24 48. A method of increasing the permeability of the apical surfaces of airway epithelial
- 25 cells to a chloride ion comprising the step of administering an agent that decreases or
- 26 inhibits the intracellular retention of mis-assembled or mis-folded glycoproteins.
- 27
- 28 49. A method of increasing the permeability of the apical surfaces of airway epithelial
- 29 cells to a chloride ion comprising the step of administering an agent that decreases or
- 30 inhibits the activity of UDP glucose:glycoprotein glycosyl transferase.
- 31
- 32 50. A method of increasing the permeability of the apical surfaces of airway epithelial
- 33 cells to a chloride ion comprising the step of administering an agent that decreases or
- 34 inhibits activity of the endoplasmic reticulum Ca^{++} ATPase.

51. A method of increasing the permeability of the apical surfaces of airway epithelial cells to a chloride ion comprising the step of administering an agent that lowers the concentration of Ca^{++} in the endoplasmic reticulum.

52. A method of increasing the permeability of the apical surfaces of airway epithelial cells to a chloride ion comprising the step of administering an agent that decreases or inhibits calnexin functional activity.

53. A method of screening candidate compounds to identify an agent that inhibits endoplasmic reticulum-associated retention or degradation of a mis-assembled or mis-folded glycoprotein, wherein the method comprises the steps of:

a). treating a cell exhibiting intracellular retention of a mis-assembled or mis-folded glycoprotein in the endoplasmic reticulum with the candidate compound; and

b). determining whether the mis-assembled or mis-folded glycoprotein is released from the endoplasmic reticulum, thereby identifying the candidate compound as an agent that causes the release of a malformed mis-folded glycoprotein from the endoplasmic reticulum.

54. A method of screening candidate compounds to identify an agent that inhibits the functional activity of UDP glucose:glycoprotein glycosyl transferase, wherein the method comprises the steps of:

a). treating a cell exhibiting intracellular retention of a mis-assembled or mis-folded glycoprotein in the endoplasmic reticulum with the candidate compound; and

b). determining whether the mis-assembled or mis-folded glycoprotein is released from the endoplasmic reticulum, thereby identifying the candidate compound as an agent that causes the release of a mis-assembled or mis-folded glycoprotein from the endoplasmic reticulum.

55. A composition which comprises two or more agents selected from the group consisting of an agent that decreases or inhibits the activity of UDP glucose:glycoprotein glycosyl transferase, an agent that decreases or inhibits activity of

- [illegible]